

Gaps in anterograde conduction in patients with the short PR interval, normal QRS complex syndrome

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SUMMARY Of 8 patients with the short PR interval, normal QRS complex syndrome studied recently, 3 reported here displayed gaps in anterograde conduction. Atrial premature beats at decreasing coupling intervals conducted with minimal AH prolongation until a zone within the cardiac cycle was reached where conduction failed at a supra-Hisian level. Conduction resumed at earlier atrial coupling intervals and was associated with a sudden increase in the AH interval and the appearance of atrial echo beats with earliest atrial activation on the proximal coronary sinus electrogram.

It is suggested that the failure of anterograde conduction at relatively late atrial coupling intervals was caused by a short AH functional refractoriness produced by the pre-excitation of the lower AV junction by a partial AV nodal bypass. Conduction resumed only when early atrial premature beats found the extranodal pathway refractory and were transmitted with decremental delay through the AV node.

Inhomogeneity of refractoriness along the length of the atrioventricular (AV) transmission system may lead to gaps in anterograde conduction (Moe *et al.*, 1965) where an atrial premature beat within a limited zone of the cardiac cycle fails to conduct anterogradely but both earlier and later atrial systoles conduct normally (Wit *et al.*, 1970a). An early hypothesis (Durrer, 1968) suggested that such 'gap phenomena' might be explained by functional longitudinal duality of conduction at a site proximal to the location of conduction block during the gap. Many examples of gap phenomena have been described (Damato *et al.*, 1976), but their explanation has not required the hypothesis of proximal dual conduction.

The syndrome of short PR interval, normal QRS complex associated with paroxysms of tachycardia (Clerc *et al.*, 1938; Lown *et al.*, 1952) provides an example of dual conduction pathways at AV nodal level (Denes *et al.*, 1974b) which is often associated with gaps in anterograde conduction (Seipel *et al.*, 1976). In this study the interplay between dual proximal conduction and distal conduction failure in 3 patients with the short PR interval, normal QRS complex syndrome is defined.

Patients and methods

During the months of March to July 1977, 8 patients with the short PR interval, normal QRS complex syndrome were admitted for electrophysiological study. Of the 8 patients, 3 had anterograde conduction gaps and their clinical details are listed in Table 1. All 3 patients had PR intervals ≤ 0.12 s and QRS complexes < 0.10 s. Two patients presented with repeated paroxysms of supra-ventricular tachycardia and the third patient suffered frequent attacks of atrial fibrillation with a rapid (180 to 240 beats per minute) ventricular response. There was no evidence of any underlying cardiac pathology or intercurrent disease in any of these patients.

Electrophysiological studies were performed in the non-sedated, post-absorptive state in the supine

Table 1 *Clinical and electrocardiographic data*

Case	Age	Sex	PR	QRS duration	QRS frontal axis	Presentation
1	50	M	0.12 s	0.09 s	+60°	Paroxysmal SVT
2	20	M	0.11 s	0.07 s	+75°	Paroxysmal SVT
3	33	M	0.12 s	0.09 s	+40°	Paroxysmal AF

SVT, supraventricular tachycardia; AF, atrial fibrillation.

position. All medications had been withdrawn at least 4 days before the study. Bipolar electrode catheters with 1 cm interelectrode distance were introduced percutaneously via the right femoral vein and positioned in the high right atrium, against the septal leaflet of the tricuspid valve and in the apex of the right ventricle. A quadripolar electrode catheter with 1 cm electrode separations was passed via a left brachial vein into the coronary sinus. Recordings were made from the distal and proximal bipoles. All signals were filtered between 50 and 700 Hz and recorded simultaneously with three surface leads: I, aVF, and V1, on an Elema Mingo-graph recorder. Time markings at 1 second intervals were superimposed on an oscillating 50 Hz baseline. Stimulation was performed with a Devices 4270 stimulator which delivered square wave pulses of 1.5 ms duration at an amplitude approximately twice the diastolic threshold. Signals were recorded during sinus rhythm and during incremental atrial pacing at rates between 100 and 160 beats per minute. Anterograde conduction characteristics were assessed by the atrial extrastimulus method in which a programmed atrial premature beat was introduced after a sequence of 8 regularly paced atrial systoles. Anterograde conduction studies were performed at several different basic pacing rates and after the intravenous infusion of 0.1 mg per kg body weight of verapamil.

DEFINITIONS

The following abbreviations, terms, and definitions are used throughout the text:

A_1 , H_1 , V_1 : The atrial, His bundle, and ventricular electrogram during basic atrial pacing.

A_2 , H_2 , V_2 : The atrial, His bundle, and ventricular electrograms produced by premature atrial stimulation.

PA : The interval between the earliest atrial activation and the intrinsic deflection of the atrial electrogram on the His bundle electrode.

AH : The interval between the intrinsic deflection of the atrial electrogram and the intrinsic deflection of the His bundle electrogram on the His bundle electrode.

HV : The interval between the intrinsic deflection of the His bundle electrogram and the earliest ventricular activation on any lead.

Anterograde conduction curve (Moe *et al.*, 1956): A graphic representation of the results of the atrial extra-stimulus technique where H_1H_2 and V_1V_2 intervals are plotted against their corresponding A_1A_2 values.

Fast (atrionodal) pathway ERP: Effective refractory period of the fast extranodal conduction pathway defined, in this report, as the shortest A_1A_2

value before the occurrence of slow pathway conduction. This interval is the lower limit of the anterograde gap in conduction during which it is assumed that concealed fast pathway conduction continues.

Fast (atrionodal) pathway FRP: Functional refractory period of the fast extranodal pathway defined as being equal to the effective refractory period of this pathway. Extranodal fibres of the type described by James (1963) or Brechenmacher (1976) are composed of atrial myocardium or Purkinje-like tissue which ordinarily does not possess decremental conduction characteristics at longer coupling intervals of A_1A_2 . A definition which involved H_1H_2 measurements would include final common pathway conduction between the site of insertion of the extranodal pathway and the point from which the His bundle deflections were recorded.

Slow (AH) pathway ERP: Effective refractory period of the slow AH conduction pathway defined as the longest A_1A_2 interval (not including A_1A_2 intervals during the anterograde gap) which is not conducted to the His bundle.

Slow (AH) pathway FRP: Functional refractory period of the slow AH conduction pathway defined as the shortest H_1H_2 interval achieved by any A_1A_2 value shorter than the ERP of the fast pathway.

Anterograde gap: A range of A_1A_2 values within the cardiac cycle where A_2 does not result in a ventricular response bracketed by zones of intact conduction.

Atrial echo zone: A range of A_1A_2 intervals in which A_2 results in a second atrial response (Ae) in which the earliest atrial activation occurs on the proximal coronary sinus electrogram.

Results

Conduction intervals during sinus rhythm are listed in Table 2. All 3 patients had short AH times (≤ 60 ms) but normal intra-atrial ($PA = 20$ -50 ms) and specialised intraventricular ($HV = 35$ -50 ms) conduction times. Incremental atrial pacing (Table 2) resulted in little or no AH prolongation.

Anterograde conduction characteristics (Fig. 1) as assessed by the atrial extrastimulus technique were abnormal in 3 respects: (1) atrial premature stimuli at progressively shorter coupling intervals resulted in minimal prolongation of the A_2H_2 time, until (2) total anterograde block developed, in all but one instance above the site from which the His bundle deflection was recorded, and (3) conduction resumed at shorter intervals of A_1A_2 with a sudden increase of the A_2H_2 interval and the simultaneous appearance of atrial echo beats or sustained tachycardia.

Recordings from case 2 are illustrated in Fig. 2.

Table 2 Conduction intervals during sinus rhythm and incremental atrial pacing

Case	Sinus rhythm			Atrial pacing	
	PA	AH	HV	100 bpm AH	160 bpm AH
1	30	55	35	55	60
2	25	45	40	45	45
3	20	60	40	60	70

Basic atrial pacing at a cycle length of 545 ms resulted in an A_1H_1 interval of 45 ms and an H_1V_1 interval of 40 ms. The QRS morphology throughout the study was that of right bundle-branch block. A_1A_2 intervals above 350 ms did not produce A_2H_2 prolongation, but as the A_1A_2 interval was reduced to 310 ms the A_2H_2 interval increased to 80 ms and anterograde block occurred below the level of the His bundle. At an extrastimulus coupling interval of 300 ms block occurred at a supra-Hisian level. Conduction resumed at an A_1A_2 interval of 260 ms with an A_2H_2 interval of 185 ms and an atrial echo beat with earliest atrial activation on the proximal coronary sinus electrogram. Further reduction in the A_1A_2 interval resulted in conduction to the ventricles with appropriate A_2H_2 prolongation and atrial echo beats with a constant H_2Ae time of 40 ms until anterograde block again occurred at an A_1A_2 interval of 220 ms.

Similar results were obtained in cases 1 and 3 with the exception that anterograde block always occurred proximal to the His bundle (Fig. 1).

Reduction in the cycle length of the basic atrial pacing sequence resulted in all patients in attenuation or abolition of the anterograde gap in conduction (Table 3) because of improved final common pathway conduction or failure of slow pathway conduction.

After intravenous verapamil, slow pathway conduction at A_1A_2 intervals less than the refractory period of the fast pathway was abolished (Fig. 3). Fast pathway conduction was not affected by verapamil.

Discussion

In 1952 Lown *et al.* reported the association between a short PR interval on the resting 12-lead electrocardiogram and paroxysms of rapid heart action. This syndrome differs from the Wolff-Parkinson-White syndrome (1930) which is also characterised by a short PR interval, in that the QRS complex is narrow. It is now firmly established that at least the majority of examples of the Wolff-Parkinson-White syndrome result from an anomalous tract of tissue which bridges the annulus fibrosus and allows pre-excitation of the ventricular myocardium by this abnormal route (Durrer *et al.*, 1970). The attenuation of the PR interval in the Lown-Ganong-Levine syndrome is the result of a short AH interval (Castellanos *et al.*, 1971; Mandel *et al.*, 1971; Neuss *et al.*, 1975) and occasionally additional shortening of the HV interval (Mandel *et al.*, 1971; Both *et al.*, 1975). By analogy with the Wolff-Parkinson-White syndrome the syndrome of short PR interval and normal QRS complex might be explained by pre-excitation of the distal AV junction by a partial or complete AV nodal bypass tract as described by James (1963) or Brechenmacher (1976) (Castellanos *et al.*, 1971; James and Scherf, 1971; Mandel *et al.*, 1971). Such a tract of tissue has been histologically verified in one patient with the short PR interval, normal QRS complex syndrome (Brechenmacher *et al.*, 1974). Nevertheless, the alternative explanation of a rapidly conducting intranodal pathway (Caracta

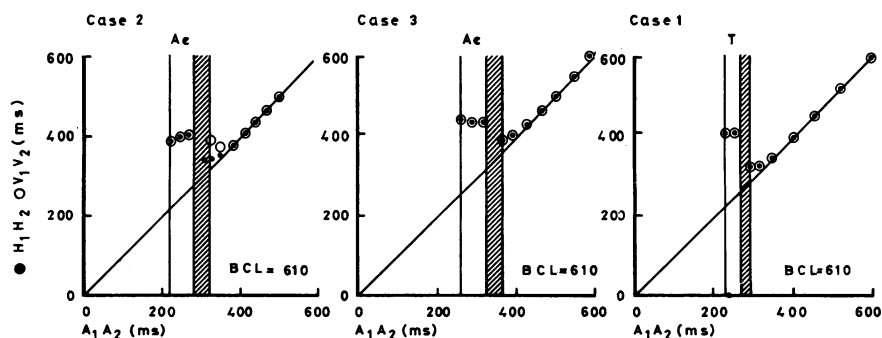


Fig. 1 Anterograde conduction curves in case 1, 2, and 3. The hatched area is the gap zone. Atrial echo zones (Ae) or tachycardia stimulation zone (T) are indicated.

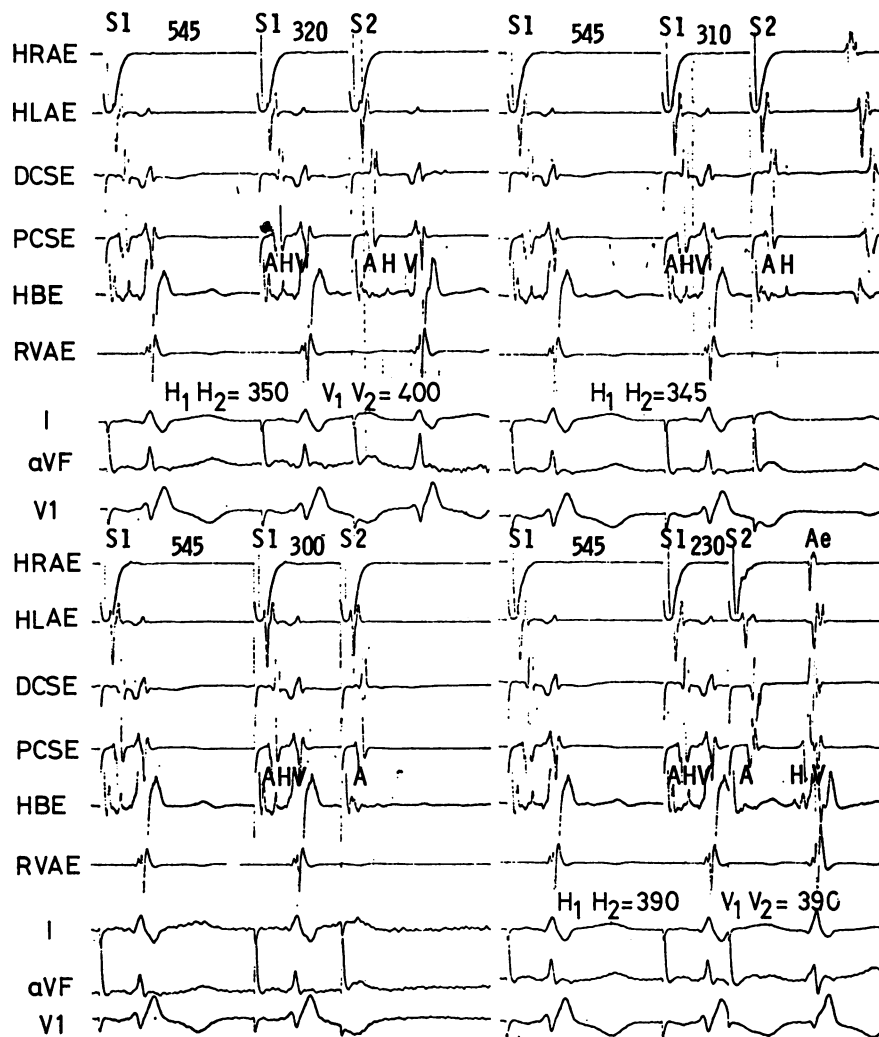


Fig. 2 Programmed atrial premature stimuli at progressively shorter coupling intervals in case 2. HRAE, high right atrial electrogram; HLAE, high left atrial electrogram; DCSE, distal coronary sinus electrogram; PCSE, proximal coronary sinus electrogram; HBE, His bundle electrogram; RVAE, right ventricular apex electrogram; I, aVF, V1, standard surface leads.

et al., 1973; Nowak and Neuss, 1974) is feasible in patients, similar to the cases reported here, with a normal HV time.

In our patients the minimal prolongation of the AH time in response to incremental atrial pacing (Bisset *et al.*, 1973; Neuss *et al.*, 1975), premature atrial stimulation (Castellanos *et al.*, 1971; Aranda *et al.*, 1976), and intravenous verapamil (Both *et al.*, 1975; Seipel *et al.*, 1976) is typical of the short PR interval, narrow QRS complex syndrome and more consistent with an extranodal bypass tract than an intranodal fast pathway. In the cases reported here,

anatomical dissociation of the fast pathway from the AV node is very likely because conduction anterogradely through the slow AH pathway results in atrial echo beats with earliest activation on the proximal coronary sinus electrode (Narula, 1974; Agha *et al.*, 1976; Amat-y-Leon *et al.*, 1976). A concealed direct VA connection is excluded because the atrial echo beat occurs before ventricular activation.

A gap in anterograde conduction is defined as a zone within the cardiac cycle where an atrial premature beat fails to be conducted to the ventricles

Table 3 Anterograde conduction characteristics at various basic atrial pacing rates

Case	Basic cycle length (ms)	Fast AH (AN)* pathway		Slow AH pathway		Anterograde gap (A ₁ A ₂)	Atrial echo zone (A ₁ A ₂)
		ERP (A ₁ A ₂)	FRP (H ₁ H ₂)	ERP (A ₁ A ₂)	FRP (H ₁ H ₂)		
1	610	290 ms	310 ms	240 ms	400 ms	265-290 ms	245-260 ms
	430	(?260) 290 ms	(?260) 310 ms	—	—	—	—
2	610	305 ms	345 ms	215 ms	380 ms	270-310 ms	220-260 ms
		(?265)	(?265)				
	545	305 ms	345 ms	220 ms	390 ms	270-310 ms	225-255 ms
		(?265)	(?265)				
	500	290 ms	335 ms	220 ms	420 ms	245-285 ms	225-240 ms
		(?240)	(?240)				
	430	290 ms	325 ms	—	—	—	—
3	610	370 ms	380 ms	260 ms	415 ms	330-365 ms	265-325 ms
		(?325)	(?325)				
	375	370 ms	385 ms	—	—	—	—

*Fast AH pathway refractory periods are measured in the conventional manner from the anterograde conduction curves. AN pathway refractoriness (effective and functional) is assumed to be the A₁A₂ interval at which conduction resumes after the anterograde gap (see text).

bracketed by zones of intact conduction. The gap phenomenon was first described by Moe *et al.* (1965) in the canine heart and subsequently extended to the human heart by Durrer (1968) and Goldreyer and Bigger (1969). Durrer interpreted his findings in terms of longitudinal duality of AV nodal conduction. Early atrial premature beats, conducting rapidly down one of two AV nodal pathways, reached the distal conduction system when it was still refractory and failed to reach the ventricles. Still earlier atrial premature beats found the fast AV nodal pathway refractory and conducted slowly down the alternate pathway to reach distal tissue after it had recovered, and conduction to the ventricles, therefore, resumed. Subsequent investigations by Wit and his associates (1970a) showed that the conduction failure of early atrial systoles occurred if the functional refractory period of the AV node was less than the effective refractory

period of the His-Purkinje system and that conduction resumed in response to very early atrial beats if sufficient proximal delay allowed the recovery of distal tissue. This explanation did not require the existence of proximal conduction system duality. Many examples of anterograde (Agha *et al.*, 1973; Gallagher *et al.*, 1973; Wu *et al.*, 1974) and retrograde gap (Akhtar *et al.*, 1974a, b) have now been described and classified in terms of sites of distal block and proximal delay (Damato *et al.*, 1976) and Durrer's (1968) original hypothesis still awaits confirmation.

Electrophysiological evidence of AV nodal dual conduction pathways is provided by the construction of an anterograde conduction curve (Moe *et al.*, 1956). The atrial extrastimulus technique is used to derive values of H₁H₂ for each A₁A₂ interval. A plot of H₁H₂ intervals against corresponding A₁A₂ values usually produces a smooth uninterrupted

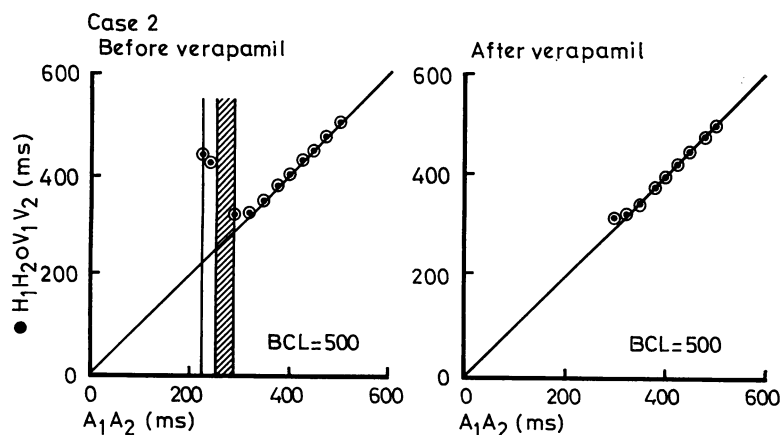


Fig. 3 Anterograde conduction curves before and after intravenous verapamil in case 2.

curve (Wit *et al.*, 1970b) but, where functional duality of AV nodal conduction is present, at critical A_1A_2 intervals, a sudden increase of H_1H_2 values may occur, when fast pathway conduction fails and slow pathway conduction is revealed (Denes *et al.*, 1973). Such discontinuous anterograde conduction plots were evident in 3 of the 8 patients with the short PR interval, normal QRS complex syndrome studied recently in our laboratory and reported here. Others have found similar results in this syndrome (Denes *et al.*, 1974b; Neuss *et al.*, 1975; Aranda *et al.*, 1976; Seipel *et al.*, 1976). The discontinuity of the conduction curves in the present cases is emphasised by the gap in anterograde conduction which separates slow and fast pathway conduction (Fig. 2). Conduction failure above the level of the His bundle may mask intermediate H_1H_2 intervals, but the slopes of the apparently separate curves suggests that they are truly discontinuous.

Duality of conduction at AV nodal level is further supported by the occurrence of atrial echo beats, with low to high atrial activation, at A_1A_2 intervals less than the effective refractory period of the fast pathway (Wu *et al.*, 1975).

Complete or partial bypasses of the AV node short-circuit the normal physiological delay imposed by the AV node. Failure of AH prolongation should result in AH functional refractoriness being limited by the fast pathway's effective refractory period. Bisset *et al.* (1975) found statistically shorter AH refractory periods in patients with short PR intervals. In our patients the functional refractory period of the fast pathway cannot be assessed from the shortest H_1H_2 interval achieved in response to atrial extrastimuli because it is uncertain where the fast pathway inserts into the AV nodal-His axis and because, during the gap in anterograde conduction, block occurs at a supra-Hisian level. Concealed fast pathway conduction probably continues during the anterograde gap zone because slow pathway conduction and atrial echo beats emerge simultaneously with the resumption in conduction. If the fast pathway's functional refractoriness is assumed to be the lower limit of the AH gap in conduction then conduction failure could be attributed, in part, to the short functional refractory period of the bypass. On the other hand, local geometric factors related to the abnormal insertion of the extranodal bypass into the normal AV nodal-His axis may be important (Janse, 1969).

Gap phenomena have been previously encountered in the short PR interval, normal QRS complex syndrome (Coumel *et al.*, 1972; Aranda *et al.*, 1976; Seipel *et al.*, 1976). Aranda and his colleagues found anterograde gaps in 2 of 4 cases reported and resumption of anterograde conduction

was not related to refractoriness of the fast pathway. Seipel *et al.* (1976) comment that anterograde gaps are frequently seen in this condition but do not mention the mechanism involved. In one illustration from their paper (Fig. 2, p. 154) conduction resumes with additional His-Purkinje delay, despite continued rapid AH conduction. In the three examples reported here the resumption of conduction is associated with an apparently sudden increase in the AH time and the simultaneous occurrence of atrial echo beats or sustained paroxysmal tachycardia.

Although conduction of premature atrial impulses at coupling intervals to the right of the anterograde gap (Fig. 1) appears to take place through a relatively fast pathway and conduction to the left of the gap through a dissociated slower pathway, the state and extent of AV conduction during the gap cannot be known with certainty because block occurs above the level of the His bundle. In case 2 at an A_1A_2 interval of 310 ms (Fig. 2) block occurs below the level of the His bundle in the presence of continued fast pathway conduction. At shorter A_1A_2 intervals conduction block occurs proximal to the His bundle. It is probable that, throughout the gap, concealed fast pathway conduction continues to depolarise the lower AV junction at a coupling interval within the refractory period of the final common pathway to the ventricles. According to this hypothesis, slow pathway conduction is prevented by the concealed depolarisation of the lower AV junction and conduction resumes when A_2 finds the fast pathway refractory and is propagated with normal delay over the slow pathway. However, if the effective refractory period of the fast pathway is at the upper limit of the AV gap, block in this pathway may have revealed a gap in which both distal block and proximal delay were confined to the slow AH pathway. The upper limit of such a gap cannot be defined and this mechanism cannot fully account for the findings in case 2 and is unlikely in the other cases. In the examples reported here, the conduction of early atrial premature beats seems related to the shift of anterograde conduction to a slow intranodal pathway (Fig. 4) reminiscent of Durrer's (1968) original hypothesis.

Anterograde conduction characteristics assessed by the atrial extrastimulus method at higher atrial driving rates resulted in attenuation and abolition of the anterograde gap. The reduction in the gap zone resulted from improved final common pathway conduction as evidenced by the reduction of the upper limit of the gap. Abolition of the gap phenomenon resulted from failure of slow pathway conduction presumably because of increased AV nodal refractoriness at higher pacing rates (Denes *et al.*, 1974a).

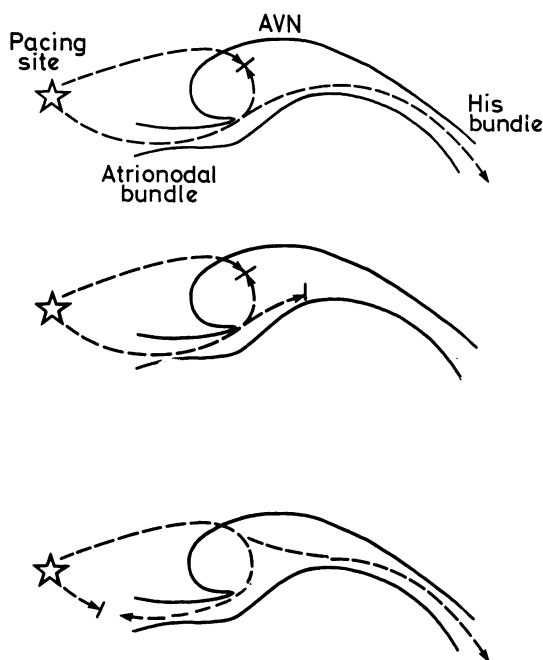


Fig. 4 Diagrammatic representation of the mechanism of gap production. Upper panel: conduction at intervals to the right of the gap; centre panel: block in AV transmission producing a gap in the anterograde conduction curve; lower panel: resumption of conduction at intervals to the left of the gap.

Verapamil does not affect atrial or anomalous bypass tract conduction characteristics, but selectively lengthens both refractoriness and conduction time of the AV node (Spurrell *et al.*, 1974; Zipes and Fischer, 1974). In all 3 patients verapamil prevented slow pathway conduction at A_1A_2 values less than the refractory period of the fast pathway thus preventing the resumption of conduction at close atrial coupling intervals and abolishing the gap phenomenon.

Anterograde gap phenomena produced by block distal to the AV node are generally masked by fast basic pacing rates and by drugs such as beta-blockers (Wit *et al.*, 1970a; Akhtar *et al.*, 1974a) and verapamil which increase AV nodal functional refractoriness. These manoeuvres cannot, therefore, be used to distinguish gap phenomena related to AV nodal duality from those produced by inhomogeneous refractoriness along the length of a single AV nodal-His Purkinje pathway.

It is seemingly paradoxical that improved conduction responsible for the short PR interval, normal QRS complex syndrome should lead to failure of conduction. Partial or complete AV nodal bypasses produce early and abnormal activation of distal

junctional tissue and add another dimension to longitudinal inhomogeneity of atrioventricular transmission responsible for the high incidence of anterograde gaps in this syndrome.

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